65. (New) The method of claim 44, for evaluating the effectiveness of a slimming treatment or care performed on a person in need thereof.

Remarks

Claims 44 to 65 remain pending after entry of this amendment. Claims 1-43 were cancelled herein. Claims 44 to 65 were added herein. Applicant would like to point out that newly presented claims 44 to 65 correspond in substance to previous claims 1 to 24. More specifically, claim 44 combines the subject matter of claims 1, 4 and 14.

Claims 4-5 and 12 are rejected under 35 U.S.C. § 112, second paragraph. Applicant respectfully traverses this rejection.

Claims 1-24 are rejected under 35 U.S.C. § 112, first paragraph. Applicant respectfully traverses this rejection.

Claims 1-2, 4-5, 7-13, and 22-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Cook et al. (U.S. Patent No. 5,855,917). Applicant respectfully traverses this rejection.

Claims 1-2, 4-5, 7-13, and 22-24 are rejected under 35 U.S.C. § 102(e) as being anticipated by Wagle et al. (U.S. Patent No. 6,326,396). Applicant respectfully traverses this rejection.

Claims 1-2, 4-5, 7-13 and 22-24 are rejected under 35 U.S.C. § 102(b) or (e) as being anticipated by Takahashi et al. (U.S. Patent No. 5,955,072) or equivalent Takahashi et al. (U.S. Patent No. 6,307,038). Applicant respectfully traverses this rejection.

Claims 1, 4-13, and 22-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Takeda et al. (U.S. Patent No. 5,244,798). Applicant respectfully traverses this rejection.

Claims 1-13 and 22-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Vainio et al. (1982). Applicant respectfully traverses this rejection.

Claims 1, 4-13 and 22-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Cheng et al. (1990). Applicant respectfully traverses this rejection.

Claims 1, 3-13 and 22-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Carroll et al. (1992). Applicant respectfully traverses this rejection.

Claims 1, 3-13 and 22-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Bensadoun et al. (1974). Applicant respectfully traverses this rejection.

Claims 1-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cook et al., Wagle et al., Takahashi et al., Takeda et al., Vainio et al., Cheng et al., Carroll et al. and Bensadoun et al. in view of NEFA-C kit from Wako. Applicant respectfully traverses this rejection.

Rejections under 35 U.S.C. § 112

Claims 4-5 and 12 are rejected under 35 U.S.C.§ 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The new claims have been drafted to avoid terms objected to by the Examiner, and have also remedied any antecedent basis issues noted by the Examiner.

Claims 1 to 24 are rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly does not reasonably provide ennoblement for comparing a putative inhibitor to a known inhibitor as a reference. The Examiner recites that it is not possible to determine the inhibitory nature of a putative compound solely on the basis of comparison to a known inhibitor.

The subject matter of previous claim 1, corresponding to new claim 44, recites in step c) that the results of the inhibition are compared to the result obtained in the absence of the potentially active substance tested or are compared with the result obtained in the presence of a known inhibitor. A person skilled in the art can choose a particular known inhibitor in order to compare the result obtained with the putative inhibitor with that known inhibitor. This choice will be made for example based on the desired purpose for the putative compound. For example, a compound that is known to have inhibitory effects useful in the field of cosmetics can be chosen as the known inhibitor if the putative compound is to be used in cosmetics.

Thus it is possible and useful to determine a certain level of inhibitory activity of this putative inhibitor on the basis of a comparison to a known inhibitor, which is more active than a control in the absence of any inhibitor. In summary, Applicant respectfully submits that the newly amended claims are enabled, and ask that this rejection be withdrawn.

Rejecti ns under 35 U.S.C. § 102

Applicant points out as a preliminary matter, that newly amended claim 44 includes the limitations of previous claim 14, which was not rejected under 35 U.S.C. § 102 over any of the references. Therefore, Applicant respectfully submits that newly added claim 44 is therefore not anticipated by any of the cited references.

The newly added claims recite a method of testing a substance which is potentially active in the field of lipolysis, the method comprising the steps a) preparing a substrate, wherein the substrate comprises at least one triacylglycerol; b) placing the substrate in contact with at least i.) a substance which is potentially active in the field of lipolysis, ii.) a lipoprotein lipase, iii.) a cofactor of lipoprotein lipase, and iv.) a fatty acid-acceptor substance or a fatty acid-sequestering substance which prevents the blockage of the enzymatic activity of the lipoprotein lipase, for a period of time sufficient for releasing, at least in part, fatty acids from the triacylglycerol; c) determining the capacity of inhibition of the release of the fatty acids resulting from the activity of the lipoprotein lipase, under the action of the potentially active substance, wherein said release of the fatty acid is monitored **using an enzymatic technique on the reaction medium**; and d) comparing said determined capacity of inhibition to a control or a reference, wherein the control is the capacity of inhibition obtained in the absence of the potentially active substance tested, and wherein the reference is the capacity of inhibition in the presence of an inhibitor known to be active in the field of lipolysis (emphasis added). None of the cited references disclose an enzymatic technique that is undertaken upon the reaction medium, and therefore none of the references anticipated the pending claims.

Cook et al. (U.S. Patent No. 5,855,917) discloses a test of the inhibition of lipase activity by conjugated ecosadienoic acid in example 3 and table 1. However this test performed by using 3T3-L1 preadipocytes and the heparin- releasable lipoprotein lipase was measured as described by Nilsson-Ehle and Schotz (1976) J. Lipid Research, 17, 536-541, here enclosed. This method uses a radioactive test instead of an enzymatic technique as currently claimed.

Wagle et al. (U.S. Patent No. 6,326,396) discloses testing for inhibition of lipoprotein lipase in example 8. However this method does not contain any fatty acid-acceptor and cofactor of lipoprotein lipase. Furthermore an enzymatic technique is not used to evaluate the inhibition.

Takahashi et al. (U.S. Patent No. 5,955,072) or equivalent Takahashi et al. (U.S. Patent No. 6,307,038) discloses a method for the determination of lipoprotein lipase inhibitory activity (in M, column 38). However this method is again based on the Nilsson-Ehle and Schotz test disclosed in Journal of Lipid Research 17:536-541 (1976) which uses a tritiated oleate glycerol to provide a radio detection with liquid scintillation counter (see column 38, line 65). Therefore, a method using an enzymatic technique is not disclosed.

Takeda et al. (U.S. Patent No. 5,244,798) discloses a method of determining the content of triglycerides in human blood based on a specific thermostable LPL produced by Streptomyces 7825 (FERM P-9983, FERM BP-2489) (column 3, lines 8-10). This document does not provide a method for the determination of the non-esterified fatty acids made upon the reaction medium by an enzymatic technique. In fact the test of glycerol formed is a titer determination based on the quantitative determination of glycerol formed through the action of LPL and does not comprise the presence of fatty acid-acceptor substance and of a LPL cofactor.

On column 7, lines 9 to 52, it is clearly disclosed that the technique used is an enzymatic assay of blood triglycerides, but this enzymatic assay is not performed on the reaction medium as is present invention. In particular, on column 4, lines 37 to 42, the fatty acid formation activity is determined by assaying an isopropanol extract and not by assaying the reaction medium. Example 2, which is cited by the Examiner, does not mention the presence of a cofactor or of a fatty acid-acceptor substance, which are both required in Applicant's invention as now claimed.

Vainio et al., Article in *Biochimica et Biophysica Acta*, 711(1982) 386-390, discloses a test of inhibition of lipoprotein lipase by benzene boronic acid with the presence or absence of apolipoprotein C-II. However, the content of released free acids is determined by a radioactive method by using tritiated oleil glycerol (see page 387, enzyme assay), and not an enzymatic technique as is required by the claimed invention.

Cheng et al., Article in *Biochem. Journal* (1990) 269, 403-407 discloses an assay of LPL which comprises the use of tritiated glycerol oleate (see page 403, assay of LPL, or materials). Carroll et al., Article in *Lipids*, Vol. 27, No. 4 (1992) disclose a similar method using a tritiated trioleate (see page 305, right hand column under the title LPL assay, lines 3-4 thereof). Bensadoun , *Journal of Biological Chemistry*, (1974) Vol. 249, No. 7, discloses a method using tritiated triolein for determining the activity of lipoprotein lipase (page 2220, under titl materials

and methods). These references also do not disclose the use of an enzymatic technique, as well as other limitations of the claims, and therefore do not anticipated the newly amended claims.

In conclusion none of the cited documents provide a method of testing a substance which is potentially active in the field of lipolysis comprising placing a substrate comprising at least one triacylglycerol in contact with a substance which is potentially active in the filed of lipolysis to be tested, with a lipoprotein lipase, a cofactor of lipoprotein lipase, and a fatty acid-acceptor substance or a fatty sequestering substance, which prevents blockage of the enzymatic activity of the lipoprotein lipase, and determining the capacity of inhibition of the released fatty acid resulting from the activity of the lipoprotein lipase, wherein the determination of the non-esterified fatty acids is determined using an enzymatic technique on the reaction medium.

Furthermore although not rejected as obvious over any of these references alone, the invention would have been nonobvious for a person skilled in the art, because of the difficulties of carrying out an enzymatic technique on a reaction medium. Especially a reaction medium utilized of the invention, that contains the fatty acid resulting from the activity of the lipoprotein lipase in the presence of a cofactor, an enzyme, and a fatty acid-acceptor substance or a fatty acid-sequestering substance like serum albumin for example.

Applicant's invention is advantageous because it avoids the use of a radioactive assay. Avoiding the use of a radioactive assay is especially important in the field of cosmetic and pharmaceutical care, because such compositions will be ingested or utilized on the subject, where it is undesirable to have radioactivity. Furthermore, the present invention provides a very simple screening method for testing numerous compounds.

Rejections under 35 U.S.C. § 103

Claims 1-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cook et al., Wagle et al., Takahashi et al., Takeda et al., Vainio et al., Cheng et al., Carroll et al. and Bensadoun et al. in view of NEFA-C kit from Wako.

Although the Examiner has not rejected the newly pending claims as obvious, Applicant notes that claim 14, which is now incorporated into new claim 44, was rejected previously, therefore Applicant will address the obviousness rejection as if it had been made with regard to the newly amended claims.

In order to establish *prima facie* obviousness, three basic criteria must be met, namely: (1) there must be some suggestion or motivation to combine the references or modify the reference teaching; (2) there must be a reasonable expectation of success; and (3) the reference or references when combined must teach or suggest each claim limitation. Applicant submits that the Office Action failed to state a *prima facie* case of obviousness, and therefore the burden has not properly shifted to Applicant to present evidence of nonobviousness.

Applicant respectfully submits that the newly added claims are not *prima facie* obvious in view of the cited references at least because the references, when combined do not disclose or suggest all of the elements. Specifically, none of the documents cited by the Examiner, either alone or in combination disclose or suggest than an enzymatic technique can be performed on a reaction medium comprising LPL, a cofactor of lipoprotein lipase and a fatty acid-acceptor substance or fatty acid-sequestering substance which prevents the blockage of the enzymatic activity of the lipoprotein lipase. Applicant agrees with the Examiner that NEFA-C kit from Wako is a well-known enzymatic technique that measures Non Esterified Fatty Acid (NEFA) colorimetrically, as shown by Takeda (US patent 5,244,798). However, Applicant asserts that it was never described to use this technique on the reaction medium. For example, in Takeda et al. (US 5,244,798), the procedure described on column 4, particularly lines 37 to 42 is that of a NEFA-C test used on an isopropanol extract formed fatty acid, such an extract would not have any proteins.

The presence of a fatty acid-acceptor substance or a fatty acid-sequestering substance and of a cofactor of lipoprotein lipase increases the difficulties of utilizing an enzymatic technique. Thus a skilled person in the art who wants to use an enzymatic technique will carry out this technique on an extract, but will not carry out this technique on the reaction medium. The inventors surprisingly discovered that an enzymatic technique for measuring the content of NEFA was efficiently working even in the presence of LPL, LPL cofactor and a fatty acid acceptor or sequestering substance. Applicant submits therefore, that it was nonobvious to utilize such a method because of the presence of a fatty acid-acceptor substance or fatty acid-sequestering substance, like bovine or human albumin.

Applicant respectfully submits in light of the newly added claims and comments offered above, that the rejection of the claims as obvious over Cook et al., Wagle et al., Takahashi et al.,

Takeda et al., Vainio et al., Cheng et al., Carroll et al. and Bensadoun et al. in view of NEFA-C kit from Wako be withdrawn and not entered with respect to the newly added claims.

Conclusion

In view of the amendments and comments presented herein, favorable reconsideration in the form of a Notice of Allowance is respectfully requested in view of new claims 44 to 65.

Respectfully submitted,
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